



MT-ND6 gene

mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 6

Normal Function

The *MT-ND6* gene provides instructions for making a protein called NADH dehydrogenase 6. This protein is part of a large enzyme complex known as complex I, which is active in mitochondria. Mitochondria are structures within cells that convert the energy from food into a form that cells can use. These cellular structures produce energy through a process called oxidative phosphorylation, which uses oxygen and simple sugars to create adenosine triphosphate (ATP), the cell's main energy source.

Complex I is one of several enzyme complexes necessary for oxidative phosphorylation. Within mitochondria, these complexes are embedded in a tightly folded, specialized membrane called the inner mitochondrial membrane. During oxidative phosphorylation, mitochondrial enzyme complexes carry out chemical reactions that drive the production of ATP. Specifically, they create an unequal electrical charge on either side of the inner mitochondrial membrane through a step-by-step transfer of negatively charged particles called electrons. This difference in electrical charge provides the energy for ATP production.

Complex I is responsible for the first step in the electron transport process, the transfer of electrons from a molecule called NADH to another molecule called ubiquinone. Electrons are then passed from ubiquinone through several other enzyme complexes to provide energy for the generation of ATP.

Health Conditions Related to Genetic Changes

Leber hereditary optic neuropathy

Several mutations in the *MT-ND6* gene have been identified in people with Leber hereditary optic neuropathy. Each of these mutations changes a single protein building block (amino acid) in the NADH dehydrogenase 6 protein. One common *MT-ND6* mutation is responsible for about 14 percent of all cases of Leber hereditary optic neuropathy, and it is the most common cause of this disorder among people of French Canadian descent. This genetic change, written as T14484C or Met64Val, replaces the amino acid methionine with the amino acid valine at protein position 64. The T14484C mutation is associated with a good long-term prognosis; affected people with this genetic change have a 37 percent to 65 percent chance of some visual recovery.

Researchers are investigating how mutations in the *MT-ND6* gene lead to Leber hereditary optic neuropathy. These genetic changes appear to prevent complex

I from interacting normally with ubiquinone, which may affect the generation of ATP. *MT-ND4* mutations may also increase the production within mitochondria of potentially harmful molecules called reactive oxygen species. It remains unclear, however, why the effects of these mutations are often limited to the nerve that relays visual information from the eye to the brain (the optic nerve). Additional genetic and environmental factors probably contribute to the vision loss and other medical problems associated with Leber hereditary optic neuropathy.

Leigh syndrome

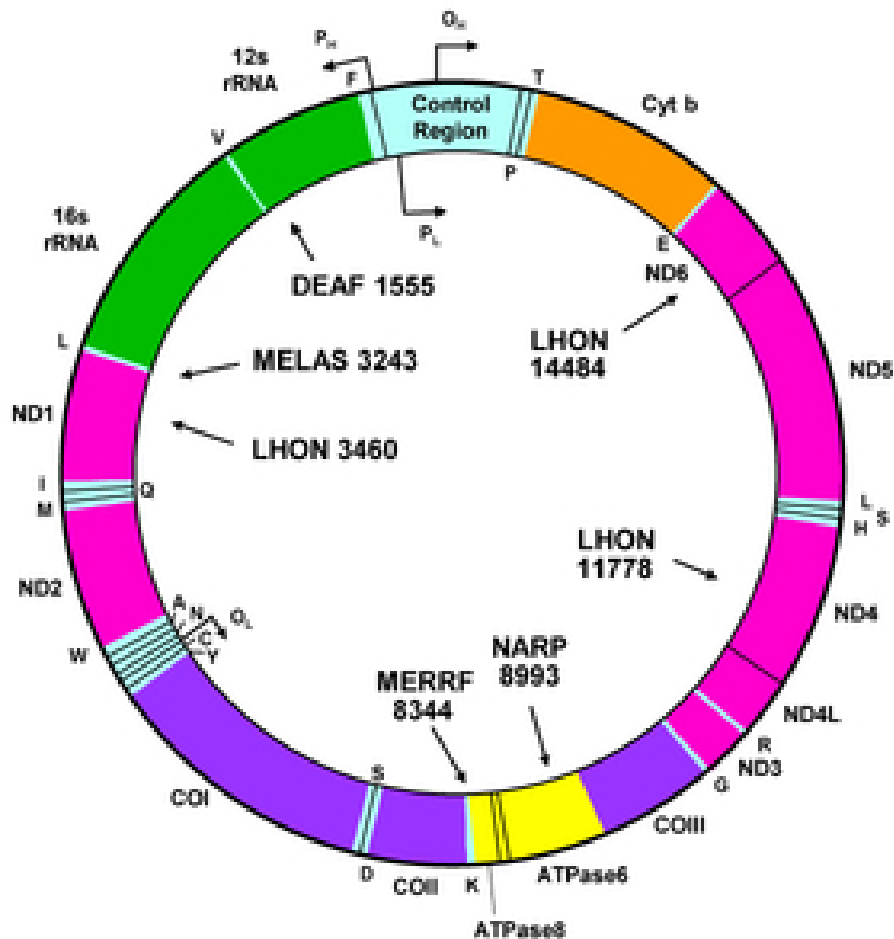
other disorders

A mutation in the *MT-ND6* gene also has been identified in a small number of people with Leigh syndrome, a progressive brain disorder that typically appears in infancy or early childhood. Affected children may experience vomiting, seizures, delayed development, muscle weakness, and problems with movement. Heart disease, kidney problems, and difficulty breathing can also occur in people with this disorder.

The *MT-ND6* mutation that can cause Leigh syndrome, written as G14459A or Ala72Val, replaces the amino acid alanine with the amino acid valine at protein position 72. This genetic change also has been found in people with Leber hereditary optic neuropathy and a movement disorder called dystonia, which involves involuntary muscle contractions, tremors, and other uncontrolled movements. This mutation appears to disrupt the normal assembly or activity of complex I in mitochondria. It is not known, however, how this *MT-ND6* gene alteration is related to the specific features of Leigh syndrome, Leber hereditary optic neuropathy, or dystonia. It also remains unclear why a single mutation can cause such varied signs and symptoms in different people.

Chromosomal Location

Molecular Location: base pairs 14,149 to 14,673 on mitochondrial DNA (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



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Other Names for This Gene

- mitochondrially encoded NADH dehydrogenase 6
- MTND6
- NADH dehydrogenase 6
- NADH dehydrogenase subunit 6

- NADH-ubiquinone oxidoreductase chain 6
- NADH-ubiquinone oxidoreductase, subunit ND6
- ND6
- NU6M_HUMAN

Additional Information & Resources

Educational Resources

- Mayo Clinic Mitochondrial Disease Biobank
<http://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview>
- Oxidative Phosphorylation (Biochemistry, Fifth Edition, 2002)
<https://www.ncbi.nlm.nih.gov/books/NBK21208/>
- The Neuromuscular Disease Center at Washington University: Complex I
<http://neuromuscular.wustl.edu/pathol/diagrams/mito.htm#complexI>

GeneReviews

- Leber Hereditary Optic Neuropathy
<https://www.ncbi.nlm.nih.gov/books/NBK1174>
- Mitochondrial Disorders Overview
<https://www.ncbi.nlm.nih.gov/books/NBK1224>
- Mitochondrial DNA-Associated Leigh Syndrome and NARP
<https://www.ncbi.nlm.nih.gov/books/NBK1173>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MT-ND6%5BTIAB%5D%29+OR+%28mitochondrially+encoded+NADH+dehydrogenase+6%5BTIAB%5D%29%29+OR+%28%28MTND6%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+subunit+6%5BTIAB%5D%29+OR+%28NADH+dehydrogenase+6%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase+chain+6%5BTIAB%5D%29+OR+%28NADH-ubiquinone+oxidoreductase,+subunit+ND6%5BTIAB%5D%29+OR+%28ND6%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>

OMIM

- COMPLEX I, SUBUNIT ND6
<http://omim.org/entry/516006>
- LEIGH SYNDROME
<http://omim.org/entry/256000>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_ND6.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=MT-ND6%5Bgene%5D>
- HGNC Gene Family: NADH:ubiquinone oxidoreductase core subunits
<http://www.genenames.org/cgi-bin/genefamilies/set/1149>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7462
- Mitomap: Leber Hereditary Optic Neuropathy Disease Mutation Database
<http://www.mitomap.org/MITOMAP/MutationsLHON>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/4541>
- UniProt
<http://www.uniprot.org/uniprot/P03923>

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